

BEST AVAILABLE COPY

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
14 December 2000 (14.12.2000)

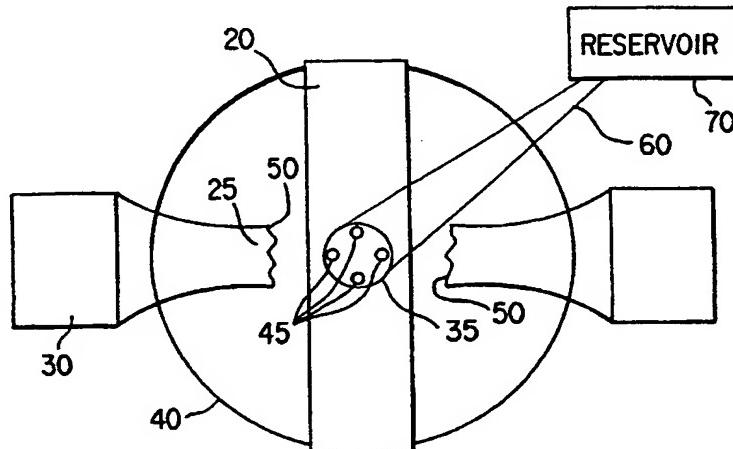
PCT

(10) International Publication Number
WO 00/74583 A1

- (51) International Patent Classification⁷: **A61B 18/20**, (10/00, 5/103)
- (21) International Application Number: **PCT/US00/15665**
- (22) International Filing Date: 7 June 2000 (07.06.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/138,193 9 June 1999 (09.06.1999) US
- (71) Applicants (*for all designated States except US*): SPEC-TRX, INC. [US/US]; 6000A Unity Drive, Norcross, GA 30071 (US). ALTEA TECHNOLOGIES, INC. [US/US]; 2056 Weems Road, Atlanta, GA 30084 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): EPPSTEIN, Jonathan, A. [US/US]; 2844 Jasmine Court, Atlanta, GA 30345 (US). MCRAE, Stuart [US/US]; 1438 Montevallo Circle, Atlanta, GA 30033 (US).
- (74) Agents: FLOAM, D., Andrew et al.; Needle & Rosenberg, P.C., The Candler Building, Suite 1200, 127 Peachtree Street, N.E., Atlanta, GA 30303-1811 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:
— With international search report.
— Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

[Continued on next page]

(54) Title: SELF-REMOVING ENERGY ABSORBING STRUCTURE FOR THERMAL TISSUE ABLATION



WO 00/74583 A1

(57) Abstract: A device to facilitate ablation of tissue, such as for forming one or more openings in the tissue for transdermal monitoring and/or delivery applications. The device comprises: (a) a support layer having at least one aperture therein, and (b) at least one energy absorbent film layer disposed over the at least one aperture in the support layer for making substantial contact with tissue through the aperture. The at least one energy absorbent film layer is under a tension force and absorbs energy focused thereon to thermally ablate the tissue. After ablation, the film layer breaks apart allowing access to the ablated tissue beneath it.

WO 00/74583 A1



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

**SELF-REMOVING ENERGY ABSORBING STRUCTURE FOR
THERMAL TISSUE ABLATION**

CROSS REFERENCE TO RELATED APPLICATION

5

This application claims priority to U.S. Provisional Application Serial No. 60/138,193 filed June 9, 1999 which is incorporated by reference in its entirety.

FIELD OF THE INVENTION

10

This invention relates to the field of tissue ablation for the formation of openings in the tissue. In particular, this invention relates to self-removing energy absorbing structures for achieving thermal tissue ablation.

15

BACKGROUND OF THE INVENTION

The flux of a drug or analyte across a biological tissue can be increased by changing the diffusion coefficient or the gradient for diffusion. Commonly, the flux is enhanced by increasing the permeability of the skin, such as by chemical penetration enhancers, iontophoresis, and poration techniques.

Thermal tissue ablation for forming openings in tissue is disclosed in commonly assigned U.S. Patent No. 5,885,211 to Eppstein, et al. There is room for improving the thermal tissue ablation process.

25

SUMMARY OF THE INVENTION

The present invention is directed to a device to facilitate ablation of tissue, such as for forming one or more openings in the tissue for transdermal monitoring and/or delivery applications. The device comprises: (a) a support layer having at

least one aperture therein, and (b) at least one energy absorbent film layer disposed over at least one aperture in the support layer for making substantial contact with tissue through the aperture. The at least one energy absorbent film layer is under a tension force over or across the aperture and absorbs energy focused thereon to thermally ablate the tissue. After ablation, and because it is under tension, the film layer breaks apart allowing access to the ablated tissue beneath it.

The present invention is further directed at a method for forming openings in a tissue comprising the steps of: (a) positioning a support layer having an aperture therein on a tissue; (b) positioning an energy absorbent film layer over the aperture to make substantial contact with the tissue through the aperture; and (c) focusing energy onto the energy absorbent film layer to conduct heat to the tissue thereby ablating the tissue.

The above and other advantages of the present invention will become more readily apparent when reference is made to the following description taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a perspective view of one embodiment of a portion of the device of the present invention.

Figure 2 is cross-sectional view taken through line A-A of Figure 1 and illustrating the relationship of the energy absorbent film to the tissue when suction is applied to the device.

Figure 3 is a top view of one embodiment of a portion of the device showing the energy absorbent film before it has been affected by energy.

Figure 4 is a top view of one embodiment of a portion of the device showing the energy absorbing layer after it has been affected by energy.

Figure 5 is a top view of one embodiment of a portion of the device used as part of a transdermal delivery system.

Figure 6 is a top view of one embodiment of a portion of the device used as part of a monitoring system.

5

DETAILED DESCRIPTION OF THE INVENTION

The present invention may be understood more readily by reference to the following detailed description of various embodiments of the invention and the
10 Figures.

Before the present articles and methods are disclosed and described, it is to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting. It must be noted that, as used in the specification and the appended claims, the singular forms "a,"
15 "an" and "the" include plural referents unless the context clearly dictates otherwise.

Ranges may be expressed herein as from "about" or "approximately" one particular value and/or to "about" or "approximately" another particular value. When such a range is expressed, another embodiment comprises from the one particular value and/or to the other particular value. Similarly, when values are
20 expressed as approximations, by use of the antecedent "about," it will be understood that the particular value forms another embodiment.

As used herein, "opening" means any size hole, aperture or pore of any depth, that is capable of substance transport therethrough. Inclusive in this term is at least one opening in the tissue sized no larger than about 1000 μm in diameter
25 called a micropore.

Throughout this application, where publications are referenced, the disclosures of these publications in their entireties are hereby incorporated by

reference into this application in order to more fully describe the state of the art to which this invention pertains.

Referring first to **Figures 1-3**, one embodiment of a portion of the present invention **100** is shown. The device **100** includes at least a support layer **7** and an energy absorbent film layer **25**. Depending on the application of the device **100**, it also includes an optional assay reagent pad **20**. The energy absorbent film layer **25** is stretched or otherwise placed under tension across a hole or aperture **40** in the support layer **7**. At least one hole or aperture **35** is provided in the assay reagent pad **20** above the hole **40** and the energy absorbent film **25**. The hole(s) **35** may be any shape or size to provide a suitable site for tissue ablation.

In one embodiment of the invention, the energy absorbent film layer **25** of **Figure 1** is held in place and under tension across the aperture **40** by at least one tension member **30**. This tension member(s) **30** may be constructed of any suitable material in any shape to create a tension force across the film **25**. In one form, at least one tension member **30** is provided at one end of the energy absorbent film layer **25** and the other end is fixed to the support layer **7** by other suitable means, such as by glue or spot weld attachment. In another form, at least one tension member **30** is provided at both ends of the energy absorbent film layer **25** to hold it under tension across the aperture **40**. Examples of materials suitable for the tension member(s) **30** include elastic, rubber, metal springs, or plastic springs or the like.

In another embodiment of the invention, tension members **30** are not needed and the film **25** is anchored directly to the support layer **7**. Such anchoring may be performed by any suitable means including adhesive bonding, electromagnetic bonding, hot plate welding, induction bonding, insert bonding, radio-frequency sealing, spot welding, thermostacking, chemical bonding, thermo bonding, vibration welding or ultrasonic welding. Examples of film **25** suitable for

such use without tension members include pre-stretched mylar, rubber, silicone, polycarbonate, polyurethane, polyvinyl chloride, or polypropylene film.

The support layer 7 serves to support the film 25 across the aperture 40. As such, suitable materials for the support layer 7 include polyester, ceramic, 5 polycarbonate (PC), polyvinylchloride (PVC), and mixtures thereof. This support layer can be of any suitable thickness to maintain structural support for the film 25.

The optional assay reagent pad 20 serves to detect the presence of a substance in the fluid. For example, the assay reagent pad 20 may be useful in detecting the presence of an analyte (such as glucose) in blood or interstitial fluid. 10 The assay reagent pad 20 may be constructed of any suitable material, with as many layers or materials as necessary for detecting the presence of a substance in a fluid. Elements of the assay reagent pad include electrodes, one or more enzymes, and one or more indicators as is well known in the electrochemical biosensor art. The assay reagent pad 20 alternatively may be a type that is optically interrogated 15 to determine a measurement of an analyte. The assay reagent pad 20 may be attached to the film 25 or may be placed proximate to the film 25 such that the pad 20 is capable of fluid communication with the film 25.

The energy absorbent film layer 25 includes a layer of material that absorbs energy and heats up. As the energy absorbent film layer 25 is heated by a beam or 20 field 10 of energy, the film 25 transfers heat to the tissue by conduction, thereby ablating the tissue. One use of ablating the tissue is to form one or more openings in the tissue for transdermal monitoring or delivery applications. Thermal tissue ablation for forming openings is described more fully in U.S. Patent No. 5,885,211.

Any suitable energy may be used for the beam of energy 10 to heat the 25 energy absorbent film 25. In one embodiment, the beam of energy 10 is a beam of optical energy, which may for example be provided by a laser diode. In another embodiment, the energy 10 is comprised of electromagnetic energy, laser, gamma radiation, and/or beta radiation, etc.

The types of energy absorbing substances that are suitable for the film 25 include those disclosed in commonly assigned U.S. Patent No. 5,885,211, and in commonly assigned PCT/0599/04929, filed March 5, 1999, both of which are incorporated herein by reference in their entireties. Copper pythalocyanine doped 5 film is an example of a suitable film 25 material. Alternatively, a clear film 25 with an absorbent adhesive layer can be used whereby the adhesive provides a positive attachment to the targeted tissue, and a thermal conduction path to the tissue. Once the aperture 40 is formed and the film 25 is retracted from the opening, the adhesive also serves to help stretch the aperture 40 and the attached 10 tissues beneath the surface, increasing the flux rate to facilitate extraction or delivery of substances via the aperture 40.

The operation of the device will now be described with reference to Figures 1-4. As shown in Figure 1, a vacuum or suction 15 is applied (by a vacuum source not shown) to a region 27 of the device 100 so as to pull the tissue 15 up to contact the film 25 through the aperture 40 of the support layer 7 (Figure 2). The film 25 flexes to provide good physical contact with the underlying tissue 5 which is desirable to achieve efficient transfer of heat to the tissue when the energy absorbent film layer 25 is heated.

The beam or field 10 of energy is then directed onto the energy absorbent 20 film 25. In response, the film 25 heats up and the heat in the film is transferred by conduction to the tissue 5, thereby ablating the tissue. As the film 25 absorbs the energy and transfers it to the tissue, eventually, because of the tension force, it breaks and separates across the aperture 40 as illustrated in Figure 4. The film 25 burns up as the thermal ablation process occurs and in so doing is weakened to be 25 overcome by the tension force. This self-removal or self-separating feature of the film 25 allows access to the ablated area of the tissue to facilitate fluid communication with the opening(s) 45 without any additional steps.

Figure 5 depicts the device 100 used in connection with a transdermal delivery system wherein at least one drug or agent is delivered to the tissue 5 via the opening(s) in the tissue 45. A reservoir 70 containing the at least one drug or agent may be in fluid communication with the opening(s) in the tissue 45 via a conduit 60, such as tubing. Alternatively, the reservoir 70 may be integrally formed with the support layer 7 so that the at least one drug or agent can be delivered into the tissue 5 in a single step procedure with gravity or pressure forcing the drugs or agents into the tissue 5.

Figure 6 shows the device 100 used in connection with a monitoring system. The assay reagent pad 20 may be located on the device 100 and connected (wired or wirelessly) to a monitoring apparatus 200. Alternatively, the assay reagent pad 20 may be located remotely in the monitoring apparatus 200 and coupled via fluid conduit 60 that carries the fluid.

Whether the assay reagent pad 20 is located remote or proximate to the opening(s) in the tissue 45 depends on the specific application. Both embodiments are useful in discrete monitoring applications for analyzing fluid on a single use basis, as well as in continuous monitoring applications for continuously extracting and analyzing fluid over a longer term basis, such as several hours, days, etc. See, for example, International Application No. PCT/US99/16378, filed July 20, 1999, entitled "System and Method for Continuous Analyte Monitoring".

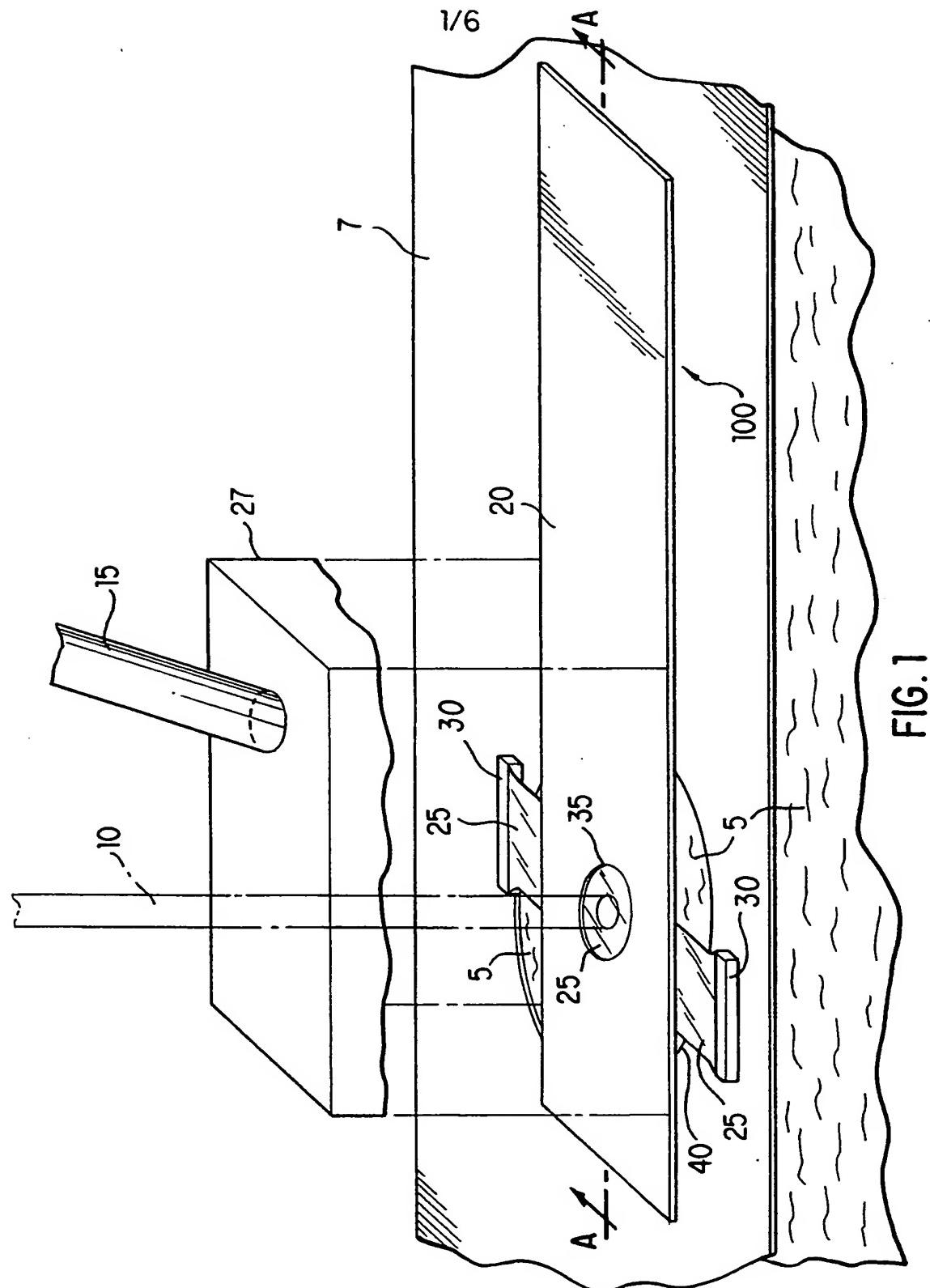
It will be apparent to those skilled in the art that various modifications and variations can be made in the present invention without departing from the scope or spirit of the invention. Other embodiments of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein. It is intended that the specification and examples be considered as exemplary only, with the true scope and spirit of the invention being indicated by the following claims.

What is claimed is:

1. A device to facilitate thermal ablation of tissue, comprising:
 - (a) a support layer having at least one aperture therein; and
 - (b) at least one energy absorbent film layer disposed over the at least one aperture in the support layer for making substantial contact with tissue through the aperture, wherein the at least one energy absorbent film layer is under a tension force; and absorbs energy focused thereon to thermally ablate the tissue.
2. The device of claim 1, further comprising an assay pad disposed proximate the aperture in the support layer.
3. The device of claim 2, wherein the assay pad has at least one aperture aligned with the at least one aperture in the support layer.
4. The device of claim 1, wherein the energy absorbent film layer heats up by absorbing energy focused thereon and conducts heat to the tissue thereby ablating the tissue and causing it to break apart over the aperture.
5. The device of claim 1, and further comprising at least one tension member that holds the at least one energy absorbent film layer under tension over the aperture.
6. The device of claim 5, wherein the at least one tension member is comprised of a member selected from the group consisting of elastic, rubber, metal springs, or plastic springs.

7. The device of claim 1, further comprising a reservoir containing at least one drug or agent for release into the tissue.
8. The device of claim 1, wherein the support layer is comprised of: polyester, ceramic, polycarbonate (PC), polyvinylchloride (PVC), or mixtures thereof.
9. The device of claim 1, wherein the at least one energy absorbent film layer is comprised of copper pythalocyanine.
10. The device of claim 1, wherein the at least one energy absorbent film layer is anchored at ends thereof directly to the support layer.
11. The device of claim 1, wherein the at least one energy absorbent film layer is flexible so as to make contact with the tissue through the aperture when vacuum is applied over the aperture of the support layer.
12. The device of claim 1, wherein the energy absorbent film layer is responsive to energy from the group consisting of; electromagnetic energy, optical energy, gamma radiation, and/or beta radiation.
13. A method for forming openings in a tissue comprising the steps of:
 - (a) positioning a support layer having an aperture therein on a tissue;
 - (b) positioning an energy absorbent film layer over the aperture to make substantial contact with the tissue through the aperture; and
 - (c) focusing energy onto the at least one energy absorbent film layer to conduct heat to the tissue thereby ablating the tissue.

14. The method of claim 13, further comprising the step of applying vacuum over the aperture to draw the tissue into substantial physical contact with the energy absorbent film layer.
15. The method of claim 13, wherein the energy absorbent film layer breaks apart to provide access to the tissue via the aperture.
16. A method for analyzing fluid collected from tissue comprising the steps of claim 13, further comprising the step positioning an assay pad in fluid communication with the tissue via the aperture.
17. A method for delivery of at least one drug or agent into tissue comprising the steps of claim 13, further comprising the step of contacting the tissue with at least one drug or agent.
18. The method of claim 13, wherein the step of focusing energy comprises focusing energy selected from the group consisting of electromagnetic energy, optical energy, gamma radiation, or beta radiation.



SUBSTITUTE SHEET (RULE 26)

2/6

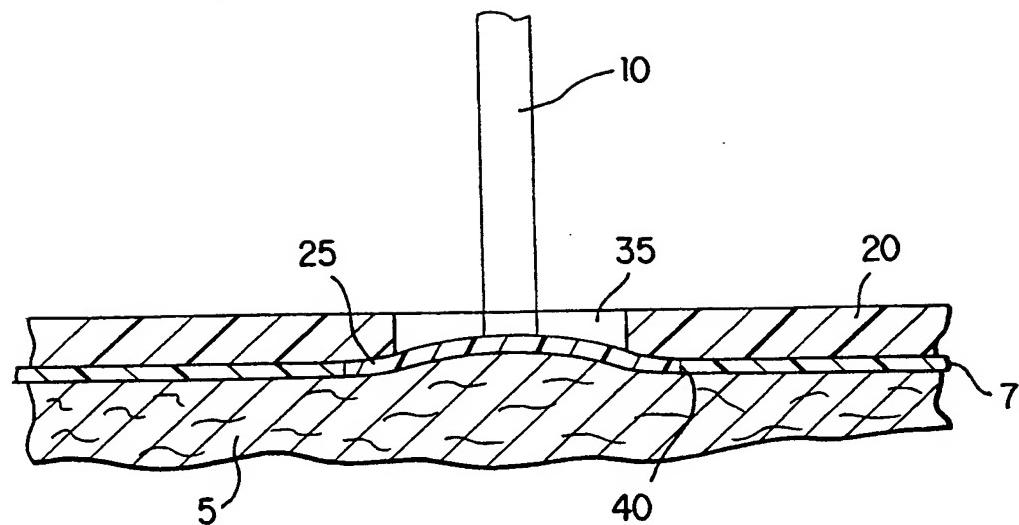


FIG. 2

SUBSTITUTE SHEET (RULE 26)

3/6

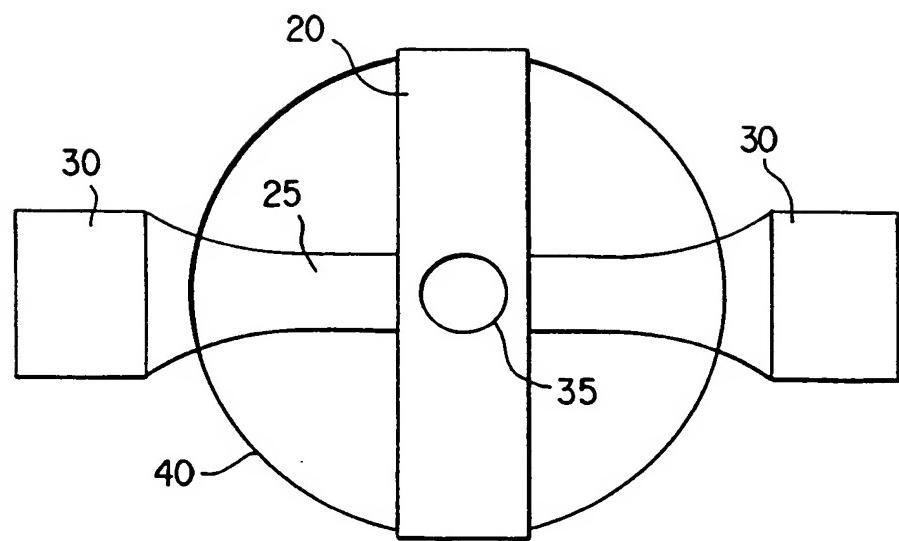


FIG. 3

SUBSTITUTE SHEET (RULE 26)

4/6

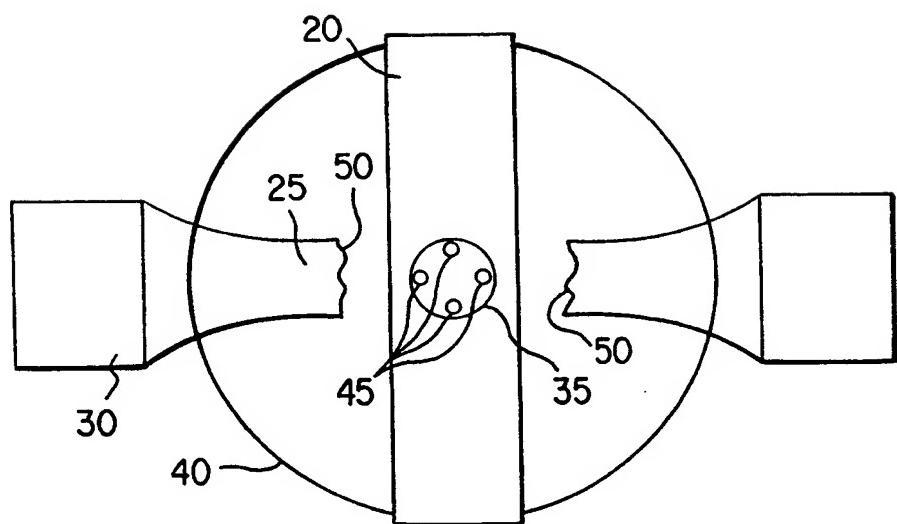


FIG. 4

SUBSTITUTE SHEET (RULE 26)

5/6

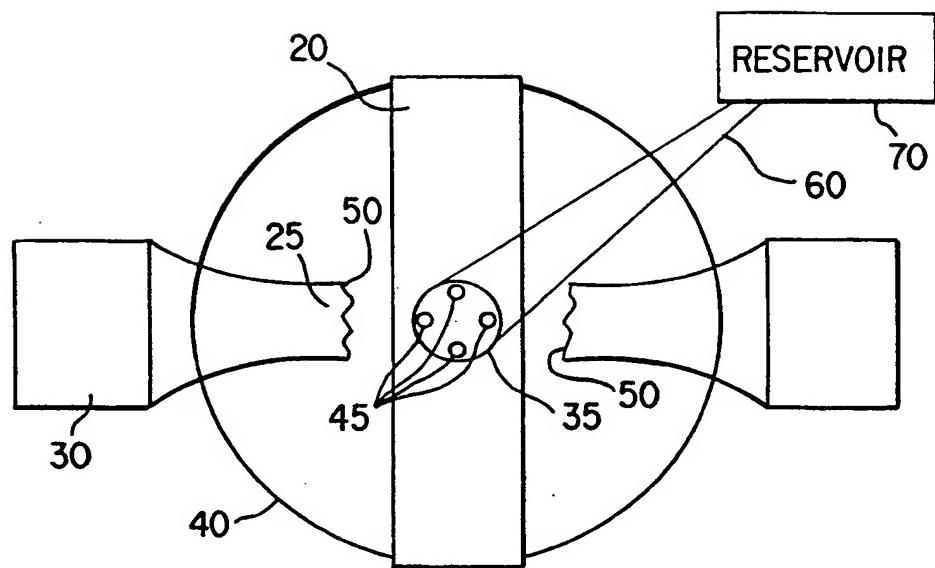


FIG. 5

SUBSTITUTE SHEET (RULE 26)

6/6

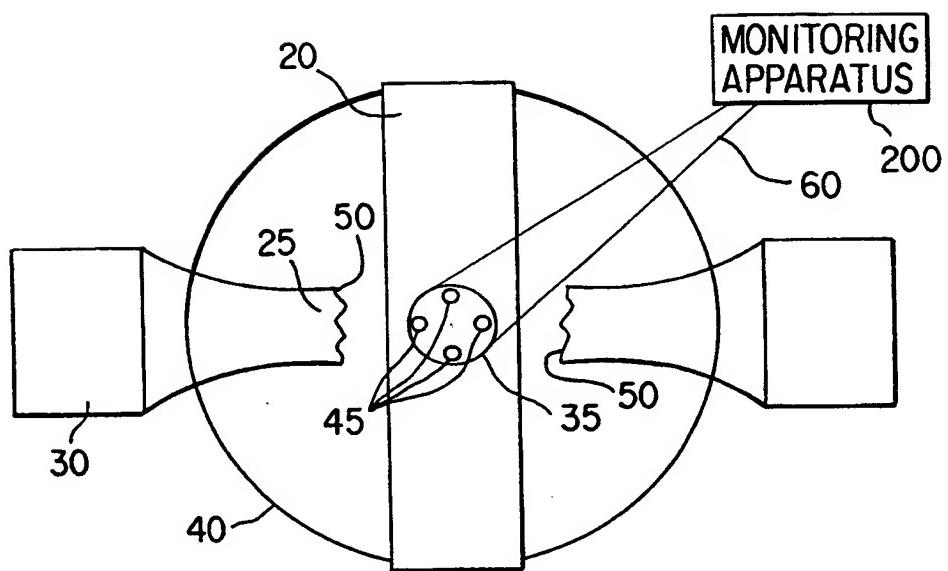


FIG. 6

SUBSTITUTE SHEET (RULE 26)

INTERNATIONAL SEARCH REPORT

Int'l Application No
PCT/US 00/15665

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B18/20 A61B10/00 A61B5/103

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 643 252 A (FLOCK STEPHEN T ET AL) 1 July 1997 (1997-07-01) column 3, line 60 -column 4, line 13; figure 2 column 7, line 38 - line 67; figures 6-8 column 9, line 1 - line 16	1,4,8, 11,12
Y	—	7
Y	WO 98 42267 A (ABBOTT LAB) 1 October 1998 (1998-10-01) page 10, line 17 - line 24; figure 1	7
A	—	1
P,A	WO 99 40848 A (ABBOTT LAB) 19 August 1999 (1999-08-19) page 7, line 24 -page 8, line 17; figures 1,2 —	1,12 —/—

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

5 October 2000

Date of mailing of the international search report

17/10/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax (+31-70) 340-3016

Authorized officer

Dureau, F

INTERNATIONAL SEARCH REPORT

Int'l Application No
PCT/US 00/15665

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 885 211 A (EPPSTEIN JONATHAN A ET AL) 23 March 1999 (1999-03-23) abstract; figure 1 _____	1
A	US 4 775 361 A (BLANK IRVIN H ET AL) 4 October 1988 (1988-10-04) column 1, line 22 - line 31 _____	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'l Application No

PCT/US 00/15665

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
US 5643252	A 01-07-1997	AU 5587694 A	24-05-1994		
		EP 0666726 A	16-08-1995		
		WO 9409713 A	11-05-1994		
		US 5839446 A	24-11-1998		
		JP 10501992 T	24-02-1998		
WO 9842267	A 01-10-1998	US 6027496 A	22-02-2000		
		EP 1011490 A	28-06-2000		
WO 9940848	A 19-08-1999	NONE			
US 5885211	A 23-03-1999	US 5458140 A	17-10-1995		
		US 5445611 A	29-08-1995		
		AU 707065 B	01-07-1999		
		AU 6863196 A	19-03-1997		
		BR 9610012 A	21-12-1999		
		CA 2199002 A,C	01-03-1997		
		CN 1195276 A	07-10-1998		
		EP 0858285 A	19-08-1998		
		GB 2307414 A,B	28-05-1997		
		HK 1009321 A	28-05-1999		
		JP 11511360 T	05-10-1999		
		NO 980878 A	27-04-1998		
		WO 9707734 A	06-03-1997		
		US 5722397 A	03-03-1998		
		US 6018678 A	25-01-2000		
US 4775361	A 04-10-1988	NONE			

THIS PAGE BLANK (USPTO)

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- FADED TEXT OR DRAWING**
- BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- SKEWED/SLANTED IMAGES**
- COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- GRAY SCALE DOCUMENTS**
- LINES OR MARKS ON ORIGINAL DOCUMENT**
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.

THIS PAGE BLANK (USPTO)